TBS and BMD at the end of AI-therapy: a prospective study of the B-ABLE cohort.

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ABSTRACT

Introduction

Patients with breast cancer under aromatase inhibitor (AI) treatment often develop osteoporosis and their average bone loss rate is twice that of natural reduction during menopause, increasing fracture risk. As the current diagnostic technique based on bone mineral density (BMD) provides no information on bone quality, the Trabecular Bone Score (TBS) has been proposed to reflect bone microarchitecture status. The present study was designed to assess prospective changes in TBS and lumbar spine (LS) BMD in postmenopausal women with breast cancer at completion of AI treatment.

Methods

B-ABLE is a prospective cohort of 735 women with breast cancer treated with AIs according to American Society of Clinical Oncology recommendations: 5 years of AI starting within 6 weeks post-surgery or 1 month after the last cycle of chemotherapy (5y-AI group), or switching to an AI to complete 5-year therapy after 2-3 years of tamoxifen (pTMX-AI group). Patients with osteoporosis were treated with oral bisphosphonates (BP). TBS and LS-BMD changes at completion of AI therapy were evaluated by Student t-test for paired samples. Pearson correlation coefficients were computed for correlations between LS-BMD and TBS.

Results

AI treatment was completed by 277 women. Of these, 70 (25.3%) were allocated to BP therapy. The non-BP-treated patients (74.7%) showed significant decreases in TBS (-2.94% in pTMX-AI and -2.93% in 5y-AI groups) and in LS-BMD (-4.14% in pTMX-AI and -2.28% in 5y-AI groups) at the end of AI treatment. In BP-treated patients, TBS remained stable at the end of AI treatment, whereas LS-BMD showed significant increases (+2.30% in pTMX-AI and +5.33% in 5y-AI groups). Moderate associations between TBS and LS-BMD values at baseline and at the end of AI treatment ($r=0.4$; $P<0.001$) were observed. At the end of treatment, changes in spine BMD and TBS were weakly correlated ($r=0.1$, $P<0.01$).

Conclusions

AI therapy induces significant decreases in TBS, comparable to BMD loss. BP-treated patients maintained TBS values, whereas BMD increased. AI treatment leads to deterioration of bone microarchitecture, which seems to be attenuated by BP therapy.

KEYWORDS

Trabecular Bone Score, Aromatase inhibitors, Oral bisphosphonates, Bone mineral density, Tamoxifen, Breast cancer

INTRODUCTION

The superiority of aromatase inhibitors (AIs) in disease-free survival compared with tamoxifen (TMX)¹⁻³ has made them the standard first-line adjuvant therapy among patients with receptor-positive breast cancer. Nevertheless, the routine use of AIs has raised concerns about their adverse effects, threatening treatment adherence⁴⁻⁶. A profound suppression of estrogen levels is derived from the potent inhibition of the aromatase enzyme caused by these drugs^{7,8}. AI-treated women often develop osteoporosis, showing an average bone loss rate twice that of the natural reduction during menopause⁹. These differences can result in a 47% increased fracture risk with AI use, compared with TMX¹⁰.

At present, bone mineral density (BMD) measured by dual X-ray absorptiometry (DXA) is the gold standard surrogate for the diagnosis of osteoporosis based on the WHO criteria¹¹. However, it is now recognized that the increased risk of non-traumatic fractures associated with osteoporosis is determined not only by the mineral content but also by bone quality and material properties, such as trabecular microarchitecture, the accumulation of microfractures, a disordered bone remodeling, or the influence of extra-skeletal risk factors¹²⁻¹⁴. Hence, the BMD measurement does not provide information on bone quality, which has been estimated to explain 70–75% of the variance in bone strength¹⁵.

The Trabecular Bone Score (TBS) is a new additional texture parameter derived from lumbar spine (LS) DXA that is postulated to reflect bone microarchitecture.¹⁶⁻¹⁸ TBS measures the rate of local variation in gray levels and is related to the structural condition of bone microarchitecture¹⁶⁻¹⁸ independently of spine and hip BMD¹⁸. Overall, in combination with BMD TBS is thought to increase the number of patients with a well-identified fracture risk¹⁸⁻²¹. A high TBS value means that the bone microarchitecture is dense, well-connected, and fracture-resistant.

Until now, the limited number of studies of AI impact on bone microarchitecture has described a larger decrease in BMD compared with TBS²²⁻²⁴.

Oral bisphosphonates (BP) have been approved as an effective antiresorptive therapy for the prevention and treatment not only of osteoporosis in normal postmenopausal women but also in

the management of AI-related bone loss (AIBL)²⁵⁻²⁸. Nevertheless, the hypothesis that BP-related BMD increases may reduce fracture risk remains controversial^{29,30}. Previous reports evaluating the skeletal preservation of BP in both healthy^{31,32} and AI-treated²⁴ postmenopausal women do not describe remarkable improvements but rather a “positive maintenance” of bone microarchitecture. However, many of them include a small sample of patients. Moreover, observations from randomized controlled trials (RCTs) may differ considerably from real-life clinical practice. Therefore, the current study was designed to assess prospective changes in TBS and BMD in postmenopausal women with breast cancer after completing AI treatment.

METHODS

Participants

From December 2005 to February 2016, Caucasian postmenopausal women diagnosed with hormone receptor-positive early breast cancer and candidates for AI treatment were consecutively recruited in the B-ABLE cohort. Postmenopausal status was defined as patients >55 years old with amenorrhea for more than 12 months, or those ≤55 with levels of luteinizing hormone >30 mIU/ml or follicle-stimulating hormone values >40 mIU/ml. Eligible participants were excluded for a history of any bone disease, rheumatoid arthritis, metabolic or endocrine diseases; prior diagnosis of Paget’s bone disease or osteomalacia; concurrent or prior treatment with BP, oral corticosteroids, or any other bone-active drug except tamoxifen.

Study design and interventions

B-ABLE is a prospective, non-selected, observational, clinical cohort study carried out at the Breast Cancer Unit and Bone Metabolism Unit, Hospital del Mar, Barcelona, Spain. Participants were treated with AIs (letrozole, exemestane, or anastrozole) according to American Society of Clinical Oncology recommendations³³: 5 years of AI starting within 6 weeks post-surgery or 1 month after the last cycle of chemotherapy (5y-AI group) or, alternatively, switching to an AI after taking tamoxifen for 2 to 3 years, to complete 5 years of hormonal therapy (pTMX-AI group).

Patients were stratified by BMD at LS, femoral neck (FN), and total hip (TH) at the outset of the study, and assigned to the corresponding therapeutic regimen: 1) those with osteoporosis

[T score < -2.5] or with a T score $\leq$ -2.0 at any site plus 1 major risk factor or prevalent fragility fractures were allocated to weekly oral risedronate or alendronate therapy (BP-treated patients) and 2) no active antiresorptive therapy in all other patients (non-BP-treated patients). All patients had a BMD assessment every 12 months until the end of AI therapy. Those who developed osteoporosis during the treatment were immediately offered oral BP treatment and were censored from the study at that point.

AI and BP treatment adherence was assessed by a specific question by the physician at each follow-up visit. Patients with low adherence (defined as medication possession ratio < 80%) were excluded from the study.

All participants were supplemented with calcium and 25(OH)vitD₃ tablets (1,000 mg and 800 IU daily, respectively), and those with baseline 25(OH)vitD deficiency (<30 ng/ml) received an additional dose of 16,000 IU of oral calcifediol (HIDROFEROL® FAES FARMA) every 2 weeks.

Variables and measurements

Bone mineral density

BMD was measured at the LS (L1–L4), FN, and TH using a DXA densitometer QDR 4500 SL® (Hologic, Waltham, MA, USA), in accordance with manufacturer recommendations. In our department, the *in vivo* coefficient of variation of this technique ranges from 1.0% at LS to 1.65% at FN.

Trabecular Bone Score

Spine TBS measurements were performed using the TBS software installed on our densitometer (TBS iNsight® v2.1, Med-Imaps, Pessac, France). The TBS is calculated on the basis of the raw data acquired in the DXA scan, evaluating the same regions of measurements as those used for the LS-BMD and without further administration of ionizing radiation to the patient.

Other assessments

Information on a large number of clinical variables was recorded at the time of enrollment, including age at recruitment, age at menarche and menopause, parity, lactation, previous

chemotherapy and radiotherapy, adjuvant treatments, weight, height, and plasma levels of 25(OH)vitD.

Ethics approval

The study protocol was approved by the Parc de Salut Mar Ethics Committee and written informed consent was obtained from all participants after they had read the study information sheet and any questions had been answered.

Statistical analyses

The primary endpoint was within-subject percentage changes in LS-BMD and TBS by the end of AI therapy. Given the observational nature of our study, the results for BP-treated and non-BP-treated patients are presented separately.

TBS and LS-BMD changes from baseline were evaluated using Student t-test for paired samples (mean $\pm$ 95%CI). To account for potential differences between the pTMX-AI and 5y-AI groups, both BMD and TBS percent changes and absolute values were examined by independent samples t-test.

By analogy with the three BMD categories, cutoff points for TBS have been previously established by a working group of TBS users from different countries: TBS ≥ 1.350 is considered to be normal, TBS between 1.200 and 1.350 is considered to be consistent with partially degraded microarchitecture, and TBS ≤ 1.200 defines degraded microarchitecture³⁴. Patient distribution throughout these TBS categories³⁴ was studied at baseline and at the end of AI treatment. Potential changes in TBS categories from baseline were assessed by marginal homogeneity tests. Pearson correlation coefficients were computed for correlations between spine BMD and TBS.

All statistical tests defined $P < 0.05$ as significant. These analyses were performed with R for Windows version 2.15.2 using the *foreign*, *ggplot2*, *reshape*, *extrafont*, *scales*, *grid* and *boot* packages and SPSS 12.0.

RESULTS

Participants

From a total of 735 recruited women in the B-ABLE cohort, 277 (37.7%) completed AI treatment and were eligible for the analyses. Of these, 70 (25.3%) were allocated to BP therapy (Fig. 1).

Figure 1: Flow-chart showing the number of patients at baseline and at the end of treatment in the B-ABLE cohort, according to BP therapy. Patients receiving 5 years of AI constituted the 5y-AI group and those switching to an AI after taking tamoxifen for 2 to 3 years correspond to the pTMX-AI group. Abbreviations: AI (Aromatase Inhibitors); BP (Oral bisphosphonates). * Scoliosis, arthrodesis, not able to position appropriately for scanning, morbid obesity.

Baseline patient characteristics are presented in Table 1.

Table 1. Baseline patient characteristics		
Patient characteristic	Non-BP-treated (n=207; 74.7%)	BP-treated (n=70; 25.3%)
Mean age (years) ± (SD)	59.8 ± 8.4	62.0 ± 8.3
Mean BMI ± (SD)	29.2 ± 5.2	26.9 ± 4.3*
Prior tamoxifen n (%)	120 (58.0%)	47 (67.1%)
Mean LS TBS (unit less) ± (SD)	1.221 ± 0.130	1.126 ± 0.114*
Mean LS BMD (g/cm²) ± (SD)	0.958 ± 0.104	0.790 ± 0.104*
Abbreviations: BP (Oral bisphosphonates); SD (Standard deviation); LS (Lumbar spine); BMI (Body mass index); BMD (Bone mineral density); TBS (Trabecular bone score). In t-test compared with Non-BP-treated group: * p<0.001.		

As expected, given the observational nature of our study, the groups differed at baseline: on average, the BP-treated patients had lower BMI, LS-BMD, and LS-TBS than those in the non-BP-treated group (p<0.001). Ten patients in the non-BP-treated group developed osteoporosis during the follow-up. These patients were immediately offered oral BP treatment and they were censored from the study at that point (Fig. 1).

Bone assessment

Mean percentage changes in LS-BMD and TBS at the end of AI treatment are summarized in Figure 2.

Figure 2: Individual percent change in TBS and LS-BMD at the end of AI treatment according to BP and previous tamoxifen treatment. Mean $\pm$ 95%CI are reported. In paired t- test from baseline: * ($P<0.05$), ** ($P<0.01$); *** ($P<0.001$). Abbreviations: AI (Aromatase inhibitors); TBS (Trabecular Bone Score); BMD (Bone mineral density); BP (Oral bisphosphonates).

Absolute TBS and LS-BMD values at baseline and at the end of treatment are detailed in Table

2.

Table 2: Absolute TBS and LS-BMD values (Mean $\pm$ SD) in postmenopausal woman with breast cancer at baseline and at the end of AI treatment according to BP treatment and previous TMX use.					
Measure	Lenght of follow-up	Non-BP-treated patients		BP-treated patients	
		pTMX-AI	5y-AI	pTMX-AI	5y-AI
TBS	Baseline	1.239 $\pm$ 0.130	1.203 $\pm$ 0.124	1.150 $\pm$ 0.104	1.078 $\pm$ 0.122*
	End of treatment	1.200 $\pm$ 0.119	1.165 $\pm$ 0.116*	1.141 $\pm$ 0.115	1.075 $\pm$ 0.133*
BMD	Baseline	0.963 $\pm$ 0.101	0.965 $\pm$ 0.106	0.808 $\pm$ 0.103	0.755 $\pm$ 0.098*
	End of treatment	0.923 $\pm$ 0.105	0.942 $\pm$ 0.110	0.825 $\pm$ 0.098	0.793 $\pm$ 0.103

Abbreviations: LS-BMD (Lumbar spine-Bone mineral density); TBS (Trabecular bone score); SD (Standard deviation); BP (Oral bisphosphonates); TMX (Tamoxifen); AI (Aromatase inhibitors). In t-test compared with pTMX-AI: * ($p<0.05$).

Non-BP-treated patients

At the end of AI treatment, significant TBS decrease was observed in both groups: pTMX-AI, -2.94% (-0.039 g/cm² [95%CI: -0.051 to -0.027]; P<0.001) and 5y-AI, -2.93% (-0.038 g/cm² [95%CI: -0.054 to -0.022]; P<0.001) (Fig. 2). An inter-group comparison did not reveal significant differences in TBS decreases between the pTMX-AI and 5y-AI groups.

Significant decreases in LS-BMD were also detected in both groups: pTMX-AI, -4.14% (-0.040 g/cm² [95%CI: -0.048 to -0.032]; P<0.001) and 5y-AI, -2.28% (-0.023 g/cm² [95%CI: -0.034 to -0.011]; P<0.001). In this case, the pTMX-AI group experienced significantly greater LS-BMD decline (-4.14%), compared to the 5y-AI group (-2.28%; P<0.05).

No significant difference was found in baseline TBS between the pTMX-AI and 5y-AI groups, whereas TBS values at the end of treatment were lower in the 5y-AI group (P<0.05). There were no significant differences in LS-BMD between the two groups at baseline or at the end of treatment (Table 2).

BP-treated patients

The TBS remained stable in both pTMX-AI and 5y-AI groups at the end of treatment (Fig.2). Compared to baseline, there was a significant increase in LS-BMD at the end of treatment in both groups, reaching +2.30% (0.016 g/cm² [95%CI: 0.001 to 0.031]; P<0.05) in the pTMX-AI group and +5.33% (0.038 g/cm² [95%CI: 0.017 to 0.059]; P<0.01) in the 5y-AI group. However, the difference between the groups in these LS-BMD gains was not significant.

Assessment of absolute measures revealed greater TBS values in the pTMX-AI group at baseline and at the end of treatment, compared with the 5y-AI group (P<0.05). Although baseline LS-BMD values were higher in the pTMX-AI group (P<0.05), the values were similar in both groups at the end of treatment (Table 2).

Changes in TBS categories

Analysis of TBS range revealed significant changes in the frequency distribution of non-BP-treated patients from baseline to the end of AI treatment (P<0.01) (Fig.3).

Figure 3: Percentages of patient distribution across TBS range at baseline and at the end of treatment, according to BP and previous tamoxifen treatment. Abbreviations: TBS (Trabecular Bone Score); BP (oral bisphosphonates).

The number of patients with degraded microarchitecture increased by 32.6% in the pTMX-AI group and by 20.5% in the 5y-AI group; in contrast, the number of patients falling within the normal range decreased by 55% and 62.5% at the end of treatment, respectively. On the other hand, no significant differences in frequency distribution throughout TBS categories in BP-treated patients were detected in either group (Fig.3). Figure 4 shows results exclusively for patients who were recategorized from baseline to the end of treatment.

Figure 4: Patients who changed TBS category from baseline to end of treatment according to BP treatment and previous tamoxifen use. Abbreviations: TBS (Trabecular Bone Score); BP (oral bisphosphonates).

At the end of AI therapy, 52/197 (26.4%) non-BP-treated patients had a decrease of one TBS category: 18/197 (9.1%) patients shifted from the normal to the partially degraded category and 34/197 (17.3%) from partially degraded to degraded microarchitecture. Only 9/197 (4.6%) non-BP-treated patients moved to a higher TBS category and 1 patient (0.5%) made an exceptional shift of two categories, from normal to degraded microarchitecture. In the case of BP-treated women, 10/70 (14.2%) patients moved up one category, while 9/70 (12.8%) fell from the partially degraded to the degraded range.

BMD and TBS correlation

Moderate associations between TBS and LS-BMD values at baseline and at the end of AI treatment ($r=0.4$; $P<0.001$) have been observed. At the end of treatment, changes in spine BMD and TBS were weakly correlated ($r=0.1$, $P<0.01$).

DISCUSSION

To our knowledge this is the first longitudinal cohort study to assess changes in TBS at the end of AI-therapy in postmenopausal women with hormone receptor-positive breast cancer. Both TBS and LS-BMD decreased significantly in non-BP-treated women. BP-treated patients showed significant increases in BMD but not in TBS. TBS and BMD reductions were more pronounced in pTMX-AI group than those in 5y-AI group. In spite of this, absolute TBS values at AI-treatment completion were similar for both groups.

Although BMD is the reference standard for osteoporosis detection and follow-up, as well as for fracture prediction, it remains subject to a set of constraints. Unfortunately, BMD does not evaluate other factors influencing bone strength, such as microarchitectural deterioration, and disproportionately evaluates cortical bone (representing 80% of bone volume), which has a relatively slow rate of turnover³⁵. These limitations can underestimate the sudden changes that might occur within the trabecular compartment. The majority of patients who sustain fragility fractures have a T-score > -2.5 ^{36,37}, there is thus an overlap between BMD values in patients with and without osteoporotic fractures^{38,39}. Therefore, the current definition of osteoporosis includes both a decrease in BMD and impaired bone microarchitecture resulting in increased bone fragility, defined as reduced connectivity of the trabecular bone structure and thinning and increased porosity of the cortical bone.

Skeletal microstructure can be assessed by techniques such as histomorphometric analysis of the transiliac crest bone biopsy, high-resolution peripheral quantitative computed tomography (HRpQCT)⁴⁰, flat-panel volume CT⁴¹, and magnetic resonance imaging (MRI)⁴². However, these procedures are either invasive or not routinely available, being limited to research purposes. TBS is a novel complementary technique for fracture risk assessment⁴³ that has been correlated with connectivity of bone trabeculae, trabecular bone volume, and compressive stiffness^{18,44}. TBS is able to distinguish between DXA scans with similar bone density^{18,45}, capturing roughly one third of fractures misclassified using BMD alone³².

In the present study, significant TBS decreases were observed in non-BP-treated patients at the end of AI treatment, both in the pTMX-AI (-2.94%) and 5y-AI (-2.93%) groups. Assuming

linearity, these reductions in TBS would correspond to mean annual rates of 1.2% (2-3 years of AI) and 0.6% (5 years of AI). The age-adjusted TBS curves reported in previous cross-sectional studies show much lower annual decline rates, even for the group of patients aged 65 years and older, in which the decrease accelerates to 0.5% per year (0.006)^{46,47}. In RCTs evaluating the effect of antiresorptive agents on TBS in postmenopausal women, annual reduction rates for the placebo groups were similar to our results^{31,32}. Regarding TBS pre-established categories³⁴, a large number of non-BP-treated women (approximately 30%) decreased by one category. Hence, the greatest number of patients belonged to the degraded microarchitecture category at the end of AI treatment.

All this suggests that AIs substantially affect bone microarchitecture. Consistent with this view, Prasad et al described mean TBS changes of -2.35% at 2 years of AI treatment⁴⁸ and Kalder et al found TBS reductions of -2.3% in exemestane-treated women over the same timeframe²³. Similarly, AI-treated patients in another retrospective cohort study experienced TBS decreases of -2.1% at a mean follow-up of 2.3 years²².

The marked reduction in estrogen levels caused by AI exacerbates the increased bone resorption and excess fracture risk induced by menopause². In our cohort, women without BP treatment showed LS-BMD decreases of -4.14% in the pTMX-AI group and -2.28% in the 5y-AI group by the end of AI treatment. Large adjuvant trials have described higher bone loss rates associated with AI treatment. For example, the ATAC trial (Arimidex, Tamoxifen, Alone or in Combination) detected LS bone loss rates from baseline to 5 years of anastrozole of -6.08%⁴⁹. Likewise, RCTs examining AI use after tamoxifen therapy have reported BMD reductions at LS of -4.16% (IES trial⁵⁰) and -5.35% (MA-17 trial⁵¹).

Overall, the average bone loss in our population was lower than previously reported. Differences in some characteristics, such as initial BMD values, may contribute to this outcome. In this sense, most of the trials mentioned report higher BMD values at baseline than those observed in our cohort, giving rise to the regression-to-the-mean bias. Moreover, the B-ABLE cohort is subject to strict monitoring not only of BMD but also of 25(OH)vitD and calcium levels. Patients in our study receive higher 25(OH)vitD supplementation^{52,53} than the Institute of

Medicine recommendations⁵⁴. Conversely, the unavailability of TBS values at the end of AI treatment in previous studies precludes a direct comparison with our data.

In the current analysis, women in the pTMX-AI group showed greater individual reductions in BMD at AI completion, compared to the 5y-AI group (-4.14% vs. -2.28%). These results are similar to those we previously described in an analysis of AI effects at 3 years of follow-up⁵⁵. Analogous findings have been detected for TBS: despite a similar reduction in TBS values at AI-treatment completion (-2.93% vs. -2.94%), we must consider that patients in the pTMX-AI group have been treated for a shorter time with AI. Tamoxifen has been shown to have partial estrogen-agonist actions in bone, exerting beneficial effects such as reducing bone resorption and stimulating bone formation in postmenopausal women with breast cancer⁵⁶. Moreover, Kalder et al demonstrated that tamoxifen induced significant sustained increases in TBS, possibly indicating a compensation and/or stabilization of bone texture parameters²³. The rebound effect of tamoxifen could be the underlying factor contributing to this phenomenon: the early increases observed not only cease with interruption of tamoxifen⁵⁷, but are also associated with a profound bone loss when switching to AI⁵⁸. Despite these findings, the pTMX-AI group in our study did not have lower mean TBS or BMD absolute values at the end of treatment, compared with the 5y-AI group.

Patients with osteoporosis or with osteopenia at high risk of fracture at baseline were allocated to BP therapy in our study. Although LS-BMD increased in both groups (pTMX-AI, +2.30%; 5y-AI, 5.33%), the TBS remained stable from baseline to the end of AI treatment. The increases in BMD values for patients in the 5y-AI group is within the range of increases reported in large trials evaluating the effects of BP on AIBL^{59,60}. The lack of statistical significance in BMD variation between groups (+2.30% vs. +5.33%) may be due to the reduced sample size.

Overall, TBS behavior in our cohort was comparable to the results obtained in the longitudinal study of Krieg et al, evaluating the effects of antiresorptive agents in TBS of older women: although TBS mimicked BMD decreases in individuals without BP treatment, it seemed to be far less responsive than BMD to osteoporosis therapy³¹. This is also applicable in RCTs monitoring the effectiveness of BP treatment, which have detected greater increases in BMD than in TBS^{24,32,48}. Moreover, the frequency of distribution throughout TBS categories for BP-treated patients was the same at baseline and at the end of AI treatment, with almost the same number

of individuals increasing (10 patients, 14.2%) and decreasing (9 patients, 12.8%) in TBS category.

In summary, antiresorptive therapy is expected to provide global maintenance of bone microarchitecture rather than major improvement. Although BPs have improved several bone parameters in some studies, the greatest improvements have been detected in patients who did not receive an AI⁶¹. The uncertainty about whether BP treatment prevents fractures in early breast cancer patients⁶² may be evidence that use of an AI can induce changes in bone microarchitecture that are more difficult to counteract by antiosteoporotic doses of BPs. The weak correlation between the changes in TBS and BMD at 5-year follow-up supports the different bone properties measured by these two techniques.

The present study has some limitations due to the prospective nature of the analysis and the relatively small sample size. Moreover, this is not a randomized controlled study, but a prospective cohort based on real-life clinical practice. Thus, in order to firmly conclude that BP therapy was the cause of the observed BMD and TBS behavior in BP-treated patients, a control group of women with low baseline BMD and without BP treatment would be required. Obviously, this is not feasible for ethical reasons. Another limitation is that the evaluation of AI and BP treatment adherence was only assessed by physician questionnaire. A strength of our study is that it was performed when AI treatment was completed and provides insights about the bone status of women with breast cancer at the end of their adjuvant therapy in real-life clinical practice.

CONCLUSIONS

In this prospective cohort study, AI treatment decreased TBS and LS-BMD to a similar extent. On the other hand, maintenance of TBS, rather than major improvement, was observed in BP-treated patients. AI treatment leads to bone microarchitecture deterioration, which seems to be partially attenuated by BPs. Larger studies are needed to determine whether the observed TBS changes are correlated with changes in fracture risk.

DECLARATION OF INTERESTS

The authors state that they have no conflicts of interest.

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